Ontario Ministry of Labour

Occupational Health and Safety Division

Occupational Health Branch

Occupational Health in Ontario

SCI. MED. DIV.

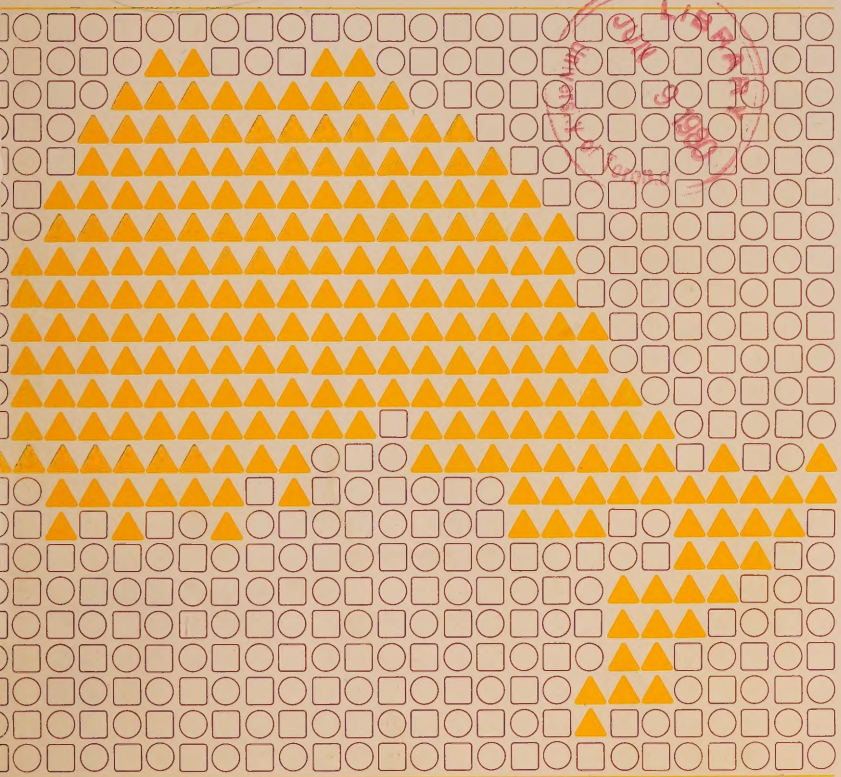
Volume 1, Number 2 April, 1980

The Ames Test – A Critical Appraisal

A Review of Aluminum Prophylaxis against Silicosis

Infrasound

Cyanide

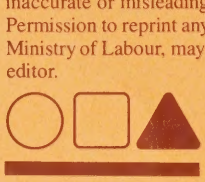


Editorial Board –

Editor
Dr. Peter L. Pelmear
Members
Miss M. Godin
Dr. Ann E. Robinson
Dr. J. Roos
Dr. G. Rosenblatt
Miss N. Quigley

Editorial Notices

While every effort is made by the publishers and editorial board to see that no inaccurate or misleading opinion or statement appears in this Journal, they wish to make it clear that the views expressed are those of the writers and do not necessarily reflect official opinion or policy. Accordingly, the publishers and the editorial board, and their respective employees, officers and agents, accept no liability whatsoever for the consequences of any such inaccurate or misleading opinion or statement.
Permission to reprint any material herein, with credit to the Ontario Ministry of Labour, may be obtained upon written application to the editor.



Occupational Health in Ontario

Volume 1, Number 2 April, 1980

SCI. MED. DIV.

Notice to Contributors

Before beginning work on a manuscript, the author should read the editorial notices carefully and prepare the typescript in accordance with the instructions given. A further check of the material should be made before it is submitted, as corrections are very expensive after the article has been set in type.

The *manuscript* should be typed double spaced with three centimetre margins on each side of the page. Two copies are required for submission to the editor, and the author should keep a copy. The manuscript should contain the following components, each to begin on a new page in this sequence: title page; summary (up to 150 words); text; acknowledgements; references; tables (each table, complete with title and footnotes, on a separate page); legends for illustration. All manuscripts will be subject to referee's approval.

Illustrations should be clearly marked on the back to show number, orientation and author's name. Photographs should be good quality, unmounted glossy prints. Original art work of line drawings and graphs should be supplied. Lettering should be large enough to allow reduction. Authors should note that typewritten lettering is unacceptable, and transfer lettering should be applied.

References in the text should be numbered consecutively in arabic numerals. All references cited should be listed in the order in which they appeared, according to the reference citation recommendations issued by the Medical Section of the Library Association.

Examples

1. Lee W.R. and Miles S. (1976): *Postgraduate preparation for occupational medicine.* Journal of the Society of Occupational Medicine 26, 115-119.
2. Department of Health and Social Security (1972): *Notes on the Diagnosis of Occupational Diseases*, rev. ed. London, HMSO, p. 19.
3. Gamble J.F. and Battigelli M.C., 1978, *Epidemiology.* Published in Clayton G.D. and Clayton F.E. (ed) *Patty's Industrial Hygiene and Toxicology*, Vol. I, New York, McGraw Hill, pp. 113-116.

Authors are advised that as a general rule it is best to give as much information in a reference and citation as possible.

Two copies of both the manuscript and the illustration should be sent to:
The Editor
Occupational Health in Ontario
Occupational Health Branch
Ministry of Labour
400 University Ave.
Toronto, Ontario
M7A 1T7

Ronald A. House
B.SC., M.D., C.M.

The Ames Test – A Critical Appraisal

Summary

A quick, inexpensive, and sensitive test is needed to determine if a chemical is a potential carcinogen. Several short term tests have been developed; the best known is the Ames Test which measures the ability of a chemical to mutate salmonella typhimurium bacteria from histidine dependent to histidine independent status. This test assumes that chemicals that are mutagens have a strong possibility of also being carcinogens and thus makes the unsubstantiated assumption that mutagenesis is a necessary pre-condition for carcinogenesis. In addition the test measures only one type of genetic damage and presents difficulties in extrapolation of results from prokaryotic bacteria to humans. Despite these drawbacks the Ames Test is an adequate de facto screening test with an estimated sensitivity of 89 percent. Furthermore the sensitivity could be magnified by using a battery of complementary short term tests to select those suspect carcinogens that require more thorough animal testing.

It is estimated that more than 50,000 different synthetic chemicals are currently in commercial and industrial use and approximately 1000 new chemicals are introduced each year. This increase in the production and use of chemicals has been especially noticeable since the early 1950s. Against this background of burgeoning chemical production are the alarming predictions of cancer epidemiologists that 80-90 percent of cancers are environmentally determined.[1,2] Many environmentally-caused cancers and also some teratogenic disorders are due to exposure to various chemicals. However of the large number of commercially used chemicals only 3000 to 4000 have been adequately tested for carcinogenicity. Hence, it is important to develop rapid, inexpensive and sensitive predictive tests to screen new chemicals and examine the large number of previously untested chemicals.

Traditionally chemicals have been found to be carcinogens by two methodological approaches – animal testing and epidemiology. There are serious limitations in the use of both these methods. Animal tests are the established means of pre-testing chemicals for carcinogenicity, but, because of the cost in skilled labour and resources, these tests usually use the minimum acceptable number of animals – perhaps two or three groups of 100 animals each – as stipulated in the United States by the National Cancer Institute standard bioassay protocol. To counteract the use of a limited number of animals, the chemical is administered at the highest dose compatible with the healthy survival of the test animal (the maximum tolerated dose, MTD) which by increasing the tumour incidence, partially offsets the statistical problems inherent in a small sample size.[3] It may be argued that the use of very high doses could distort the pattern of metabolic pathways in the test species and give abnormal results. Other drawbacks of animal tests are their expense (currently $250,000 per chemical for a thorough test), and their duration (two to three years). Because of these factors, reports for adequate cancer tests are published on only about 150 previously untested chemicals each year. Therefore, animal testing is an untenable means for screening new

chemicals and the backlog of untested chemicals in current use.

Epidemiology is a second method for the detection of chemical carcinogens. At this time it is the most reliable test system for determining the carcinogenicity of chemicals in human beings.[4] However, it is usually done on a post-hoc or retrospective basis. Many environmentally-induced cancers have a long latent period of 20 to 40 years which means that a carcinogen may not be detected until many years after exposure. Also, it is often difficult to connect cause and effect using epidemiologic methodology. For example, it would be difficult to detect the presence of a small increase in a commonly occurring cancer due to a widely used chemical. The difficulty in finding adequate records to build up complete exposure histories is an added complication.[5] Hence neither epidemiology nor animal testing can be used as a primary tool for the rapid testing of potential chemical carcinogens.

A third method – short term tests of the effects of chemicals on microorganisms or mammalian tissue culture cells – has been developed in recent years. In general these tests use the identification of bacterial, yeast, insect or mammalian cell mutation, or malignant cell transformation of mammalian cells in culture as an aid to predict chemical carcinogenicity. There are a variety of these quick, inexpensive tests but the best known, most widely used and most extensively validated is the Ames Test developed by Bruce Ames of the University of California. This is essentially a test of the ability of a chemical to induce point mutation in bacteria.

Point mutation refers to the alteration in the nucleotide sequence of a single gene, as opposed to more generalized types of genetic disruption such as chromosome breakage.

Protocol of the Ames Test

In the Ames Test, the test organism is a strain of salmonella typhimurium bearing a mutation (his^-) that prevents it from producing one of the enzymes required for the synthesis of the amino acid histidine. It therefore requires the addition of histidine (histidine auxotroph) to its growth medium. A small amount of histidine is added to the medium to allow the production of a background lawn of bacteria on the culture plate. Spontaneous back mutation (reversion to histidine independent status) can be identified and enumerated because only the revertant bacteria form discrete

colonies against the background lawn. The spontaneous rate of reversion which is usually very low can be considerably enhanced if the his^- bacteria are exposed to a chemical that induces mutations. This is the theoretical basis for the Ames Test.

The test itself is performed by combining on a petri plate the chemical to be tested, about one billion salmonella typhimurium bacteria of a particular test strain, and homogenized liver extract from rats (or less commonly from human autopsy). This latter component, the S9 microsomal fraction, is added because most carcinogens are usually pre-carcinogens and require metabolic activation by microsomal mixed function oxidases to become carcinogenic. The co-factors necessary to assist mixed function oxidase activity are also added to the test system. After incubation at 37°C for two days the number of bacterial revertant colonies is recorded. Each colony is composed of the descendants of a bacterium that has mutated from a defective histidine gene to a functional one. A value greater than .01 revertant colonies per nanomole of chemical is considered to be a positive test result.[6]

Obliteration of the background lawn of bacteria indicates a severe toxic effect with death of all bacteria tested. In this case the test is repeated with lower (subtoxic) concentrations of the chemical. The importance of adding a trace of histidine to the growth medium to generate a background lawn of bacteria is therefore self-evident.

Validation of the Ames Test

Ames claims that the results of this test on 300 chemicals reported as carcinogens or non-carcinogens on previous animal experiments has validated the test as a good predictor of carcinogenicity. About 90 percent (157 out of 175) of known animal carcinogens with a broad range of chemical structures caused mutation in the salmonella test. For known or suspected human carcinogens, 89 percent (16 out of 18) were positive. Approximately 87 percent (94 out of 108) known non-carcinogens in animals were negative.[7,8,9] The non-carcinogens fell into two general categories: 62 chemicals most of which were fairly closely related and even isomeric to carcinogens, and 46 common biochemicals. All 46 common biochemicals showed no mutagenic activity. From these studies and corroboration by similar results from independent researchers,[10] Ames concluded that mutagenesis had been validated

as a test of carcinogenesis because a very high percentage of carcinogens were found to be mutagens and a similarly high percentage of non-carcinogens were non-mutagens. However the remaining unknown factor is the percentage of mutagens which are carcinogens. Also, although there is a high correlation between carcinogenicity and mutagenicity, the relationship may be fortuitous, not causal, and fraught with significant exceptions.[11]

Objections to the Ames Test

There have been numerous objections to the Ames Test. These may be classified as follows:

1. Objections based on genetic factors

The salmonella assays measure only point mutation – either base pair substitution or frameshift mutations. However the types of potential genetic damage which may result from exposure to mutagenic agents are extremely diverse and include not only point mutation but also (a) alterations in chromosome structure (b) alterations in chromosome number (aneuploidy, polyploidy); (c) stimulation of unscheduled DNA synthesis; (d) inhibition of DNA repair (e) increased mitotic recombination between homologous chromosomes. Therefore the use of a single genetic endpoint lessens the sensitivity of the Ames Test, and additional research will be required to provide assays for classes of genetic damage which cannot be detected with the Ames Test.[12]

2. Objections based on metabolic factors

Most carcinogens are actually pre-carcinogens and do not initiate cancer directly, but require metabolic activation to become carcinogens. On the basis of numerous studies on metabolic activation the Millers suggested that most if not all chemical carcinogens are electrophilic compounds or must be converted or activated to an electrophilic state before they can initiate cancer.[13] A number of chemical carcinogens exist which are electrophilic and do not require further activation. These include alkylating agents such as mustard gas, bischloromethyl ether and the nitrosoureas. However the majority of chemical carcinogens are relatively inert and require metabolic activation to exert their carcinogenic effect.[14] The metabolic reactions involved are usually part of the normal detoxification process. Most detoxifying reactions are

catalysed by enzymes, known as mixed function oxidases, localized in varying concentrations in the endoplasmic reticulum (microsomal fraction) of a wide variety of cells, tissues and organs. The liver has a particularly high concentration of these enzymes. Usually oxidation leads to the production of innocuous and more water soluble derivatives which are either directly excreted in urine or bile, or conjugated to other endogenous compounds like glucuronic acid prior to excretion.

The activity of the mixed function oxidase enzymes is influenced by many factors including age, sex, nutritional status, presence of enzyme inducing agents and heredity; hence there is considerable intra species variation in pharmacological or toxicological response (including carcinogenic response) to foreign chemicals. Also species differences in sensitivity to a particular carcinogenic chemical can be related in some cases to the ability or failure of the species to metabolize the pre-carcinogen to a reactive metabolite. Finally, organ specificity or organotropic effects of chemical carcinogens probably can be accounted for in many instances by the type and concentrations of various microsomal enzyme systems present in the particular organs.[15]

In vitro studies of the metabolism of foreign chemicals may not be indicative of true in vivo metabolism. In the Ames Test, the S9 rat liver fraction may not adequately reflect human in vivo activity because: (a) there may be species variation in liver enzymatic activity; (b) the activating enzymes may be present in organs other than the liver; and (c) two or more activating steps may exist, and not all steps may be localized in the liver.

3. Objections based on other physiological variables affecting the concentration of a suspect carcinogen in a target organ.

In the Ames Test exposure of bacterial DNA to a test chemical only requires penetration of the chemical through the bacterial cell membrane. However, in man and other animals the chemical must first be absorbed, be distributed to the target organs, traverse cellular membranes, bypass cytoplasmic detoxification systems and then penetrate the nuclear membrane before reaction with DNA has any possibility of occurring. All of these variables are important in determining the final concentration of the test substance in the nuclei of the cells of the target organs. These variables are not considered in the Ames Test.

4. Objections to tacit assumptions about cancer etiology made by the Ames Test.

In effect, the Ames Test assumes that mutagenesis is a necessary and sufficient condition for carcinogenesis. This assumption is inconsistent with existing knowledge of cancer etiology and pathogenesis. Mutagenesis may not always be a necessary condition for carcinogenesis. Ten percent of known animal carcinogens are negative in the Ames Test. Some quite potent animal carcinogens such as dimethylaminoazobenzene and urethane are not mutagenic with or without a liver enzyme system present. Mutagenesis is quite definitely not a sufficient pre-condition for carcinogenesis. Indeed the pathway from altered (? mutated) stem cell to cancer is extremely complex with a myriad of endogenous (especially hormonal and immunological) and exogenous factors, and promoters modulating the development of cancer. This complex and multifaceted model of cancer pathogenesis is made light of by the litmus paper quality of the Ames Test.

Benefits of the Ames Test

Despite all of these drawbacks, the Ames Test still has many benefits. These include:

1. Duration of the test

The test is very rapid – it takes only two days to perform

2. Cost

It is relatively inexpensive – the average cost per chemical is only about $70.

3. It is an adequate de facto screening test

Despite the fact that the Ames Test makes unsubstantiated assumptions about the etiology of cancer (i.e. that mutagenesis is a necessary pre-condition for carcinogenesis) it has a tested sensitivity of 90 percent for animal carcinogens. This makes it a useful de facto screening device to select those chemicals which are potential carcinogens so that they can then be subjected to more rigorous animal tests. The screening sensitivity may be augmented by combining the Ames Test with other complementary short-term tests as part of a total battery of tests. No single short-term test is perfect; each system detects a few carcinogens that others do not. Hence combining the Ames Test with a cell transformation tissue culture test and/or other short-term tests would probably provide more meaningful and sensitive results. Heddle and Bruce favour the combination of the in vitro Ames Test and the in

vivo sperm abnormality assay as a battery for screening those agents which may affect human germ cells.[16] Considerable work remains to be done in developing the right combination of in vitro activation systems and test strains to be used in the battery to allow for comprehensive evaluation of possible routes of chemical metabolic activation and types of endpoint genetic alterations. A study being conducted under the auspices of the International Association of Environmental Mutagen Societies is currently assessing individual tests to determine where tests duplicate each other and where they make unique contributions.[17,18] Validation of the test battery should be regarded as an ongoing process so that tests may be dropped or added as experience dictates.[19,20]

This battery of tests or indeed one highly sensitive single test like the Ames Test will then have numerous practical applications. It may easily be used for identifying mutagenic components in complex mixtures such as air and water pollutants, and impurities in complex commercial products. This would be extremely expensive and laborious if animal testing were used. Furthermore the Ames Test may be useful for detecting weak carcinogens which would be difficult to identify by animal tests or epidemiology because of statistical limitations.

4. Contribution to theoretical knowledge

From a purely research perspective the test system may help to clarify basic mechanisms of action of chemical carcinogens, and help to elucidate the active metabolic forms of chemical carcinogens.

5. Potential use of the Ames mutagenic potency index in standard setting

Ames and others, notably Meselson and Russel, have attempted to establish a direct relationship between mutagenic potency of a chemical in the salmonella test and carcinogenic potency in laboratory animals. For 10 of 14 known chemical carcinogens investigated by the latter two individuals there was a positive correlation.[7,21] This suggests that mutagenic potency (total number of revertant colonies per nanomole of chemical) may be a helpful adjunct in standard setting for those carcinogens indispensable in current use. Certainly this could never be the sole criterion because the process of standard setting involves an amalgam of scientific and technical data as well as political, social and economic considerations. However it is conceivable that at some point in the future the Ames muta-

genic potency index, or some other type of microorganism based mutagenic potency index might be one of many important factors considered in the process of standard setting.

To summarise, despite its numerous limitations the Ames Test provides a quick, inexpensive and quite sensitive method of screening new and currently used industrial and commercial chemicals. The sensitivity of screening could be magnified by using a battery of complementary tests, and this will probably be the most important and useful application of the Ames Test – as a part of a test battery to select those suspect carcinogens which require more thorough animal testing. Other uses such as incorporation of the Ames mutagenic potency index into the standard setting process are still in the formative stages, and will require considerable elaboration before being considered for practical use.

Requests for reprints should be addressed to:
Dr. Ronald A. House,
Medical Consultant,
Occupational Health Branch,
Ministry of Labour,
1 West Avenue South,
Hamilton, Ontario.
L8N 2R9.

References

[1]Weisburger, J.H. 'Environmental Cancer.' *Journal of Occupational Medicine*. Vol. 18, No. 4, April, 1976, p. 245-252.

[2]Wynder, Ernst L. and Gio B. Gori. 'Contribution of the Environment to Cancer Incidence: An Epidemiologic Exercise.' *J. Natl. Cancer Inst.*, Vol. 58, No. 4, April 1977, p. 825-834,

[3]Clayson, David B. 'Relationships Between Laboratory and Human Studies.' *Journal of Environmental Pathology and Toxicology*, 1977, Vol. 1, p. 31-40.

[4]Markert, Clement L. ed. *Cancer: A Problem of Developmental Biology*. Prentice-Hall Inc. New Jersey, 1978. p. 88-121.

[5]Levy, Leonard S. 'Testing Chemicals for Cancer Risk,' *Occupational Health*, Sept. 1976, p. 442-445.

[6]Ames, Bruce N. and Joyce McCann. 'Carcinogens are Mutagens: A Simple Test System,' in Montesano et al ed. *Screening Tests in Chemical Carcinogenesis*, IARC Sci. Publ. #12, 1976, p. 493-499.

[7]Ames, Bruce N. 'Identifying Environmental Chemicals Causing Mutations and Cancer,' *Science*, Vol. 204, 11 May 1978, p. 587-593.

[8]McCann, Joyce et al. 'Detection of Carcinogens as Mutagens in the Salmonella/Microsome Test: Assay of 300 Chemicals.' *Proc. Nat. Acad. Sci. U.S.A.* Vol. 72 No. 12, Dec. 1975, p. 5135-5139.

[9]McCann, Joyce and B. Ames, 'Detection of Carcinogens as Mutagens in the Salmonella/Microsome Test: Assay of 300 Chemicals: Discussion.' *Proc. Nat. Acad. Sci. U.S.A.* Vol. 73, No. 3, March 1976, p. 950-954.

[10]Sugimura, Takashi et al. 'A Critical Review of Submammalian Systems for Mutagen Detection.' In D. Scott et al, ed. *Progress in Genetic Toxicology.* Elsevier/North – Holland Biomedical Press, 1977, p. 125-140.

[11]Rohrborn, G. 'Mutagenesis and Carcinogenesis.' In Montesano, R. and L. Tomatis ed. *Chemical Carcinogenesis Essays*, IARC Scientific Publication #10. Lyon, 1974, p. 213-216.

[12]DeSerres, Frederick J. 'Strength and Weaknesses of Microbial Test Results for Predicting Human Response.' *Journal of Environmental Pathology and Toxicology*, 1977, Vol. 1, p. 43-48.

[13]Miller, Elisabeth C. and James A. Miller. 'Biochemical Mechanisms of Chemical Carcinogenesis.' In Harris Busch, ed. *The Molecular Biology of Cancer.* Academic Press: New York, 1974, p. 377-397.

[14]Boyland, E. 'Biochemistry of Occupational Cancer.' *J. Soc. Occup. Med.* 1977, Vol. 27, p. 97-101.

[15]Gardner, Colin R. 'Carcinogenic Activation and the Biological Detection of Activated Metabolites,' *J. Soc. Occupational Medicine,* (1979), 29, p.54-60.

[16]Heedle, John A. and W. Robert Bruce. 'On the Use of Multiple Assays for Mutigenicity, Especially the Micronucleus, Salmonella and Sperm Abnormality Assays.' In D. Scott et al ed. *Progress in Genetic Toxicology.* Elsevier/North – Holland Biomedical Press, 1979, p. 125-140.

[17]'International Study of Short-Term Carcinogenicity Tests.' *Editorial Comment. Nature*. Vol. 274, Aug. 24, 1978, p. 740-741.

[18]Hay, Alastair. 'Short-term tests can predict potential carcinogens, says study.' *Nature,* Vol. 282, Dec. 13, 1979, p. 664.

[19]Bridges, B.A. 'Use of a Three-Tier Protocol for Evaluation of Long-Term Toxic Hazards Particularly Mutagenicity and Carcinogenicity.' In R. Montesano et al ed. *Screening Tests in Chemical Carcinogenesis*, IARC Sci. Publ. #12, 1976, p. 493-499.

[20]DeSerres, Frederick J. 'Long Range Planning for Effective In Vitro Tests for Carcinogenesis.' From R. Montesano et al ed. *Screening Tests in Chemical Carcinogenesis*' IARC Sci. Publ. #12, 1976, p. 29-39.

[21]Devoret, Raymond. 'Bacterial Tests for Potential Carcinogens.' *Scientific American*, Aug. 1979, Vol. 241, No. 2, p. 40-49.

John Wilson
B.SC., M.L.S.

Infrasound

Summary

The term 'infrasound' is usually used to describe acoustic vibrations and frequencies below about 20 Hz. There are many sources of both natural and man-made infrasound. The reported biological effects of infrasound include complaints of a non-specific nature resembling reactions to mild stress or alarm and behavioural or psychological effect. Great personal variability and degree of response to infrasound is also reported. There are few exposure limits for infrasound and none in Canada. No exposure above 150 dB should be allowed and ear plugs are strongly recommended for all intense infrasound exposures. All data support the tentative conclusion that infrasound which is not subjectively perceived in some way has no effect on performance, comfort and general well-being.

Introduction

The term, 'infrasound' is usually used to describe acoustic vibrations and frequencies below about 20 Hz.

Prior to the 1960s, infrasound was the subject of very few academic studies because instruments with only limited capability for measurement were available. Even today there are many unanswered questions regarding the possible ill effects of infrasound.

Definition

There are basically three kinds of human exposure to vibration, namely:

a) media borne vibrations transmitted simultaneously to the whole body surface or substantial parts of it. This occurs when the body is immersed in a vibrating medium such as air or water. Since the wavelengths range upward from about 50 metres in air, infrasound falls into this category.

b) contact borne vibrations transmitted (1) to the body as a whole through the supporting surface usually to the feet or buttocks. This type of vibration is usual in vehicles, vibrating buildings and around working machinery and is known as whole body vibration; or (2) to particular parts of the body such as the head or limbs, for example, vibrating powered tools and hand appliances. This type of vibration is known as segmental vibration.

It is important to differentiate these different types of vibrations since they occur under different circumstances and have different effects upon the body. Two or more of these types of vibrational energy may coexist in the work place.

Although normally inaudible, infrasound can be heard if present at very high intensities. The hearing thresholds of various frequencies of infrasound are given in Table I.

Table 1

Binaural thresholds for whole-body stimulation (Yeowart and Evans, 1974) from twelve observers.

Frequency (Hz)	Threshold (dB re 0·0002 μ bar)	Standard error of mean
20	85.2	0.6
15	92 1	0 4
12	97 0	0 6
10	99 5	0.6
8	102.4	0.7
5	111.1	0 6
4	112.4	0 8
2	121.4	0.5

Sources

1) Natural

Infrasound occurs in nature at relatively low intensities. Sources of natural infrasound are:[1]

a) earthquakes
b) volcanic eruptions
c) winds
d) air turbulence
e) thunder
f) large waterfalls
g) waves impacting upon the shore

2) Man-made

Man-made sources of infrasound include:

a) air conditioning, heating and ventilation systems
b) transportation systems in vehicles
c) blast furnaces
d) oil fired boilers
e) compressors

Figures 1, 2, 3, and 4 below show noise spectra measured in several occupational/environmental environments. Studies have shown that the maximum intensity level of infrasound in industry is about 135 dB[3].

Figure 1

Boiler house noise (5% bandwidth analysis).

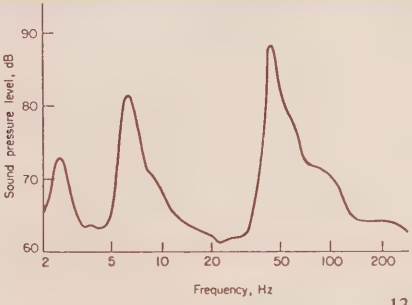


Figure 2

Noise close to a blast furnace (5% bandwith analysis).

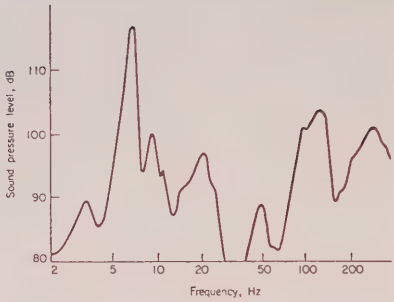


Figure 3

Noise in a small office. x – -x before treatment; o – o after treatment (one-third octave bandwidth analysis).

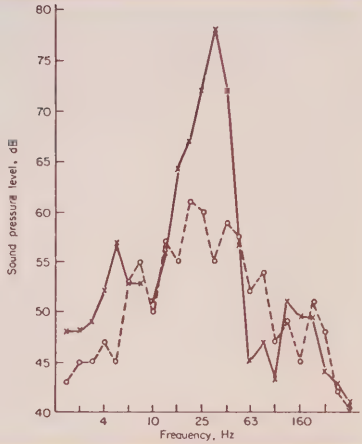
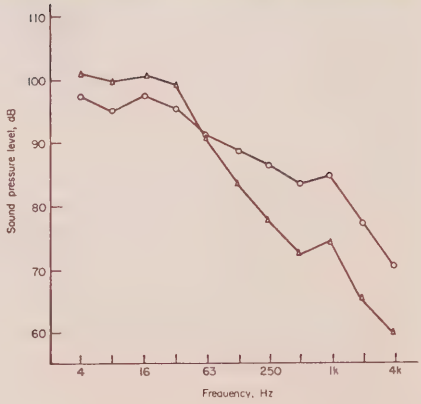


Figure 4

Octave band spectra obtained in cab of a new 32 tonne tractor unit. Δ – Δ 48 km/h; o – o 80 km/h.



Effects on man

Several investigators have examined the biological effects of intense infrasound[4, 5, 6, 7, 8, 9, 10, 11]. The reported effects include complaints of a non-specific nature resembling reactions to mild stress or alarm and behavioural or psychological effects. Green and Dunn[6] showed a correlation between the occurrence of natural infrasound and an increased rate of automobile accidents and increased absenteeism in school children and unskilled workers. There are also suggestions[10] that so called, 'psychogenic illness' may in fact be caused by infrasound although at present there is insufficient experimental or epidemiological evidence to verify this.

The claimed ill effects of infrasound may be aural or whole body. The aural effects (measured by exposure to infrasound through headphones) are said to include:

a) temporary threshold shift (TTS) across most frequencies
b) permanent ear damage due to concussive effects (only at extremely high intensities)
c) nystagmus, ie. regular rolling movement of the eyes in response to stimulation of the vestibular system
d) tinnitus (ringing of ears) and
e) middle ear pain

The reported whole body effects are as follows:
a) post-exposure fatigue
b) temporary decrease in blood levels
c) increase in heart rate
d) increase in respiration rate
e) trembling or shivering
f) decrease in muscle tone
g) post-exposure headaches
h) build-up of middle ear pressure
i) drowsiness
j) giddiness
k) chest wall vibration
l) difficulty in speaking and voice modulation
m) nausea
n) dyspnea
o) sensations of fear
p) modifications of EEG (alpha wave)
q) reaction time effects

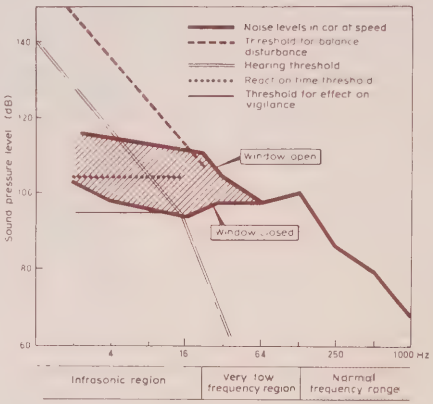
There is some controversy whether these symptoms are caused by the fundamental infrasound waveform or by the contaminating higher order harmonics[10]. Reinish found that he could divide his experimental

subjects into a sensitive group and a non-sensitive group based on their alpha wave response[10]. Great personal variability and degree of response to infrasound is also reported[5]. One suggestion is that persons susceptible to motion sickness are also sensitive to infrasound since many of the reported symptoms of exposure to infrasound (headache, fatigue, nausea and dizziness) are well known motion sickness phenomena.

Figure 5*

The heavy lines trace the noise levels inside a British one litre saloon car travelling at 60 mile/h. Also shown are the thresholds of infrasound levels affecting vigilance, reaction time and balance; and the hearing threshold. Even with the driver's window closed, the level of infrasound is enough to affect his vigilance; with it open his reaction time is increased, and for a small percentage of drivers a disturbance to balance is possible.

*(Bryan and Tempest, 1972)



The graph in Figure 5 illustrates the noise spectrum measured in a small automobile travelling at 60 miles per hour[4]. Also indicated are the thresholds at which infrasound effects vigilance, balance and reaction time. The author suggests that infrasound may be a cause of motor vehicle accidents. Infrasound levels in trucks are generally at the level of 95 – 115 dB (See Figures 6 and 7)[2].

Noise-experienced personnel wearing hearing protectors can tolerate infrasound at pressure levels of up to 150 dB for up to two minutes without threat to safety or well being[12]. One of the more perplexing aspects of infrasound investigation is that while some experiments show profound effects as listed above, others show no effect for exposures of up to 30 minutes duration.

Figure 6

Octave band spectra in a 32 tonne tractor unit showing effect of opening one cab window.
x – -x 48 km/h; o – o 80 km/h. Full lines, windows closed; broken lines, one car window open.

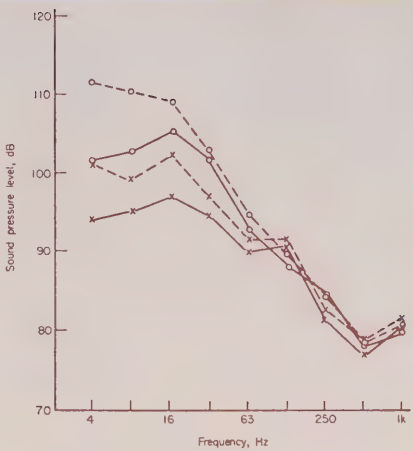
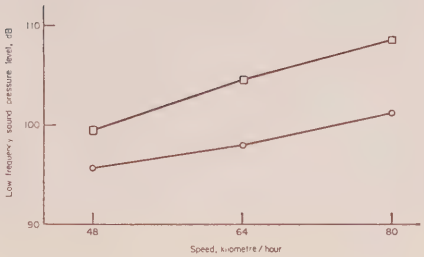


Figure 7

Mean infrasound levels in lorry cabs (4-32 Hz octave bands, three lorries) as a function of speed.
□ – □ windows open; o – o windows closed.



Exposure limits

The auditory system appears to be more sensitive to adverse effects of infrasound than any other system evaluated except possibly for whole body response at intense exposure levels. Thus, defining limits in terms of the auditory system should also provide protection to other body systems and functions.

There are exposure limits for infrasound in few jurisdictions and none in Canada. Exposure limits have been suggested by von Gierke and Nixon[2]. They were derived with respect to safety and preservation of bodily functions. Subjective annoyance or discomfort was not taken into consideration. These limits are illustrated in Tables 2 and 3, and Figure 8. It should be noted that the harmonics, where they occur, fall within the normally audible range of frequencies and are subject to the corresponding exposure limits. No exposure above 150 dB should be allowed and ear plugs are strongly recommended for all intense infrasound exposures. These limits were arrived at by assuming that exposure at 20 Hz for eight minutes has no effect at levels up to 141 dB, and by using the equal energy rule of 3 dB per doubling or halving of exposure time.

It must be kept in mind that these limits were not established with respect to comfort and annoyance, and that exposure to these levels of infrasound would not preclude symptoms of discomfort.

Table 2

Table of recommended maximum permissible exposures

Duration (hr)	Frequency (Hz)			
	1	5	10	20
1	145	138	135	132
8	136	129	126	123
24	131	124	121	118

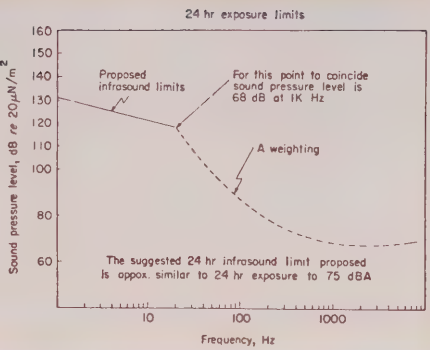
Table 3

*Duration (minutes)	Frequency (Hz)		
	1-7	8-11	12-20
8	150	145	140

*16 hours rest between exposures

Figure 8

Recommended limit levels of infrasound for 24 hr exposures.



Hearing protection[2]

It is well known that ear plugs can provide good attenuation across the audio frequency range. In contrast, earmuff protector performance decreases with decreasing frequency. Subjective reports of ear protector effectiveness in intense infrasound exposures indicate that good insert-type ear plugs can provide appreciable attenuation of the acoustic energy of infrasound. Earmuff-type protectors appear to provide negligible protection and may even exacerbate the problem due to their vibration against the side of the head during infrasound exposure[13]. For optimal protection in sound fields below 20 Hz, good insert-type ear plugs are recommended for short duration exposures; good insert-type ear plugs in combination with good earmuffs are recommended for intense exposures of long duration.

Discussion

Typical noise control strategies often muffle high frequency sounds by producing low frequency noises (including infrasound) of equal intensity but reduced loudness.

Transportation is perhaps the most important area where infrasound may affect workers. Levels up to 120 dB have been measured in road and rail transport, in helicopters and in ships' engine rooms.

Although experimentally produced infrasound at 120 dB can cause vestibular problems, etc., as outlined above there is little evidence that these effects occur in real life situations. Below 130 dB any hazard to the ear is unlikely.

There are not many comfort criteria on man's exposure to infrasound. Situations where reported subjective adverse effects have been directly correlated in a causal way with infrasound exposure are rare. Some case studies in which workers or residents felt uncomfortable, oppressed or ill-at-ease during occupational or environmental exposure to infrasound have been documented.[2]

To date, all studies have been concerned with short term exposures with relatively high intensities, and have not been long term or investigations of exposures to real life levels of infrasound. All data support the tentative conclusion that infrasound which is not subjectively perceived in some way has no effect on performance, comfort and general well-being.[2]

Requests for reprints should be addressed to:
John Wilson,
Occupational Health Hazard Analyst
Standards and Programs Branch
Occupational Health and Safety Division
Ministry of Labour
9th Floor
400 University Avenue
Toronto, Ontario
M7A 1T7

Acknowledgements:
I wish to thank W. Tempest for permission to use Tables 1 and 2, and Figures 1-4 and 6-8 from Infrasound and Low Frequency Vibration.

References

[1]Environmental Protection Agency. (1973) *Public health and welfare criteria for noise*, Washington.

[2]Tempest, W. ed. (1976) *Infrasound and low frequency vibration*. Academic Press: New York, pp. 1-36.

[3]International Labour Office. (1976) *Noise and Vibration in the working environment*, Geneva: International Labour Office.

[4]Bryan, M.E. and Tempest, W. (1972) *Does infrasound make drivers 'drunk'?* New Scientist 16 March. pp. 485-586.

[5]Evans, M.J. and Tempest, W. (1972) *Some effects of infrasonic noise in transportation*. J. Sound and Vibration V. 22, pp. 19-24.

[6]Green, J.E. and Dunn, F. (1968) *Correlation of naturally, occurring infrasonics and selected human behaviour.* J. Acoustical Society of America. V. 44, November pp. 1456-1457.

[7]Hood, R.A., Leventhall, A.G. and Kyriakides, K. (1972) *Some subjective effects of infrasound*. Proceedings British Acoustical Society V. 1, No. 3, paper 71-107.

[8]Mohnr, G.C. et al. (1965) *Effects of low frequency and infrasonic noise on man.* Aerospace Medicine V. 36 No. 9, pp. 817-824.

[9]Nixon, C.W. *Some effects of noise on man*. (1971) Proceedings of 1971 Intersociety Energy Conservation Engineering Conference.

[10]Reinish, S.M. (1979) *Some differential effects of infrasound on humans*. Paper presented at the 14th meeting of the Canadian Neurological Association, June 1979.

[11]Stephens, R.W.B. and Bryan, M.E. (1971) *Annoyance effects due to low frequency sound*. Proceedings of Fall meeting of British Acoustical Society. Paper 71-109.

[12]Tempest, W. ed. (1976) *Infrasound and low frequency vibration*. Academic Press: New York, pp. 115-150

[13]Nixon, C.W., Hille, H.E. and Kettler, C.R. (1967) *Attenuation characteristics of earmuffs at low audio and infrasonic frequencies*. Aerospace Medical Research Laboratory. TR No. 67-77, May, 1967.

Murray Finkelstein
Ph.D., M.D.

A Review of Aluminum Prophylaxis against Silicosis

Summary

This paper reviews the evidence for the use of aluminum prophylaxis against silicosis and the possible health hazards involved. It is concluded that there is circumstantial evidence of its benefit and little of any harmful effects from the type and concentrations of aluminum used.

There was some controversy in the media during the autumn of 1979 concerning the practice of aluminum prophylaxis for the prevention of silicosis. This technique, employed by many mines in Ontario, involved the spraying of aluminum powder into mine change rooms in the belief that inhalation of finely divided aluminum powder would prevent the development of lung scarring by silica dust inhaled during mining operations. As a result of union requests, the practice was suspended pending review. In this article we will examine some of the issues involved in aluminum prophylaxis.

History of Aluminum Prophylaxis

Silica is a major constituent of the earth's crust and appears in varying quantities in the ore-bearing rocks of Ontario. When silica dust is deposited in the lungs, the particles of silica are engulfed by scavenger cells (macrophages) in an attempt to remove them from the lung. Unfortunately, silica is toxic to these cells and they are killed, releasing both the dust particle and their packets of corrosive enzymes. This leads to a chain of events in which the dust particles are engulfed by a succession of macrophages, each of which is killed and releases its contents of enzymes. As a result of this cell killing and corrosive action, scar tissue is formed in the lungs and deterioration occurs in the capacity to oxygenate blood. The affected individual notes a sense of breathlessness and decreased capacity for physical activity. The degree of damage produced is related to the amount of silica inhaled and individual susceptibility.

In 1926 silicosis was made a compensable disease in Ontario, and it became apparent that silicosis was a major problem in provincial miners. In 1932 a research effort was begun by McIntyre Mines, in co-operation with the University of Toronto, to find a method to prevent silicosis. The researchers felt that the toxicity of silica was related to its solubility in body fluids and began their research with the hope that if the solubility

of silica retained in the lung could be reduced sufficiently by the addition of some non-toxic element or compound, then the usual fibrotic response would be modified. In 1936, Denny and Robson of McIntyre mines discovered that, when examined in the test tube, small amounts of metallic aluminum almost completely prevented silicious material from passing into solution. This discovery provided the impetus for the large scale animal experiment reported upon in 1939. In their experiments Denny, Robson, and Irwin exposed groups of rabbits to dusts of aluminum alone, silica alone, and silica plus aluminum. At autopsy, the aluminum controls appeared free of lung damage and the rabbits breathing silica alone were noted to have varying degrees of silicosis. In those rabbits breathing both silica and aluminum, there appeared to be no sign of silicosis. It appeared that the solubility theory was proven correct, and that aluminum could prevent silicosis.

It thus seemed that a potentially useful treatment had been discovered. To investigate the question as to whether aluminum dust itself might be harmful to humans, Crombie and Blaisdell visited the Aluminum Company of America and examined X-rays of the men working in exposure to aluminum dust. They found no evidence of occupational lung disease in these men. They returned to Ontario and treated a small group of men with aluminum inhalations and claimed that the men felt subjectively improved. On the basis of the promising experimental work in animals and the lack of evidence for toxicity in humans, the aluminum treatments were introduced into Ontario mines, and by 1945 they were used in all the gold mines in Ontario. The recommended dose was a ten-minute inhalation of tumble-milled aluminum powder at a concentration of 35 mg per cubic meter of air.

Issues

The major issues of contention with respect to aluminum prophylaxis are: (a) Is it of any benefit? and (b) Is it harmful? We will examine each of these questions in turn.

Question of Benefit

1) Animal experiments:
Inhalation experiments have been performed in a variety of animal species including rabbits, rats, and guinea pigs by a number of research teams in Europe and North America. All these experiments have demonstrated that aluminum powder inhalations have an effect in diminishing or retarding the damaging effects of inhaled silica dust. Since the damage produced in animals' lungs by silica appears similar to the pathology produced in human lungs, it seems reasonable to assume that the observed protective effect of aluminum in animals might occur in human lungs as well.

2) Human experience:
The incidence of silicosis in Ontario miners has been declining over the past 40 years. (An exception occurred in the group of men employed in the Elliott Lake uranium mines.) Since the use of aluminum treatments has overlapped in time with improved dust conditions in the mines brought about by engineering controls, it is impossible to say what effect, if any, the use of aluminum has had. At the time of introduction of the treatments it was felt that they were a major health benefit which should not be withheld from any of the men. In retrospect, it appears that the creation of both a treatment group and a control group would have enabled researchers to quantify the degree of benefit or of harm associated with the treatments. It will be very difficult, if not impossible, to answer this question with the data currently available. The situation at present is that aluminum inhalations are of no *proven* benefit in the prevention of silicosis.

Question of Harm

Concern has been expressed about the possibility that aluminum itself may cause damage to lung tissue and produce disabling disease. Researchers have also recently become interested in the possible role of aluminum in neurological diseases such as Alzheimer's Disease, an early form of senility.

1) Animal experiments:
Inhalation experiments in animals have failed to find any evidence for aluminum-induced lung fibrosis. Aluminum appears to act as a nuisance dust, stimulating an outpouring of scavenger cells.

2) Human experience:
There were reports from Germany during the Second World War of a fibrotic lung disease occurring in workers employed in factories manufacturing flake aluminum powders for explosives. Dust conditions were poor in these factories and exposures were heavy. The aluminum was processed by hammering and the final product was a fine flake-like powder. Several cases of lung disease were also reported from two factories in England producing a similar product.

Surveys at major aluminum producers in Britain and North America have failed to disclose evidence of lung disease. The declining incidence of pneumoconiosis in Ontario mines is indirect evidence that powdered granular aluminum produced by grinding must have low or absent lung toxicity. Pathologists examining the lungs of deceased miners at autopsy have found no sign of aluminum-related damage. The changes observed have been those characteristic of silica damage.

In analyzing the available evidence, there is an indication that the flake-type of aluminum produced by stamping may produce lung fibrosis. All the indications are, however, that granular aluminum is of minimal toxicity, or is completely harmless.

Neurological disease

An alarming and usually fatal neurological disease has been observed in recent years in a number of patients treated for kidney failure with hemodialysis, and this syndrome has come to be known as dialysis encephalopathy. Several research teams have measured higher tissue levels of aluminum in the brains of these patients than in the brains of patients dying of other causes. It is not yet known whether aluminum is the cause of the disease or whether it happens to collect in brain tissue damaged by another mechanism. Many of these patients are treated with large doses of aluminum-containing medication and absorb as much aluminum in one week as miners would inhale in one year. In order to reach the brain, inhaled aluminum dust would have to dissolve in body fluids and circulate in the blood. A fraction of this absorbed aluminum would be filtered by the kidneys and excreted in the urine. It is unknown, at present, whether miners have elevated levels of aluminum in their brains.

A research team at the University of Toronto has suggested that aluminum might be associated with

cases of early senility. At the moment this is a research hypothesis and is being actively investigated.

To date miners have not been studied for neurological disease, and this would likely be an unrewarding investigation because of the nature of the intellectual changes and the influence of confounding factors, such as alcohol consumption.

Conclusions

Aluminum prophylaxis was introduced into Ontario mines during the 1940s on the basis of experiments in animals which showed that aluminum inhalations prevented silicosis and a survey at the Aluminum Company of America which failed to find any signs of aluminum toxicity. The incidence of silicosis in Ontario miners has indeed fallen but, because of simultaneous improvements in dust conditions, it is impossible to say what influence the aluminum inhalations have had.

There is evidence from Europe that high concentrations of flake-aluminum powder may produce lung fibrosis. There is no evidence that the granular powder inhaled in mine prophylaxis produces lung disease, and animal experiments have been negative.

The role of aluminum in neurological disease remains to be clarified. The amounts inhaled in a prophylaxis program are similar to the amounts ingested in a typical North American diet and so the risk, if any, is not likely to be great.

In conclusion, there is no proof in humans that aluminum powder inhalations retard or prevent silicosis. There is, however, circumstantial evidence for its benefit based on the results of experiments with animals. There is little, if any, indication that the type and quantity of aluminum powder used in prophylaxis programs is harmful to man.

Requests for reprints should be addressed to:
Dr. Murray Finkelstein
Special Studies & Services Branch,
Ministry of Labour,
8th Floor, 400 University Avenue,
Toronto, Ontario.

References

A detailed bibliography concerning the issues involved in aluminum prophylaxis may be obtained upon request from the author.

Ihor Taraschuk
M.A.Sc.,M.D.

Cyanide

Summary

This paper discusses the signs, symptoms and treatment of cyanide poisoning. Cobalt EDTA is advocated as the antidote of choice. The more traditional treatment of sodium nitrite followed by sodium thiosulphate is also discussed. Since the use of these drugs may have serious medical consequences, it is felt that the decision to use them should rest with the attending physician.

The extreme toxicity of cyanide is due to its ready reaction with the trivalent iron of cytochrome-oxidase ($Cyt - Fe^{3+}$). The role of this enzyme in cellular oxygen utilization is inhibited by the formation of a cytochrome oxidase-cyanide complex. The resultant cytotoxic hypoxia leads to cellular dysfunction and death.[1] The manifestations of poisoning vary from headache, tachypna, and excitement; to vomiting, hypotension, convulsions, coma and cardio-respiratory arrest. It should be noted that the early signs of cyanide poisoning are similar to anxiety, and this must be distinguished from real anxiety which will certainly be present if the patient believes he has been exposed to cyanide. It is essential therefore that a good medical history be obtained before treatment is initiated and that antidotes be used only in patients who are unconscious or losing consciousness. All other patients require close observation and evaluation before antidotes are used. It should be stressed that intensive care is critical and that a 'bitter – almond smell' may or may not be present.

Treatment

The desired chemical reaction is:

$$Cyt - Fe\ CN \rightarrow Cyt - Fe^{3+} + \text{bound cyanide}$$

(non-functional enzyme) → (functional enzyme) + (bound cyanide)

In this reaction cytochrome oxidase is liberated from the cyanide ion (CN) and therefore allowed to partake in oxygen dependent metabolism. This may be accomplished in the traditional way with nitrite and thiosulphate or by the use of Cobalt EDTA.

a) Use of Nitrite and Thiosulphate

The traditional treatment regimen has been to administer a nitrite by inhalation of amyl nitrite perles, followed by the intravenous injection of 10 mls of 3 percent sodium nitrite. An intravenous infusion of nore-

pinephrine has sometimes been necessary to maintain blood pressure. After the administration of the sodium nitrite, 50 mls of 25% sodium thiosulphate needs to be injected intravenously.[1] The purpose of this treatment is to produce methemoglobin (ferric ion):

$$Hb - Fe^{2+} + NaNO_2 \rightleftarrows Hb - Fe^{3+}$$

(Hemoglobin) $\rightleftarrows$ (methemoglobin)

The methemoglobin competes with the cytochrome oxidase ($Cyt - Fe^{3+}$) for the cyanide ion. Since the concentration gradient favors methemoglobin, cyanmethemoglobin ($Hb - FeCN$) is formed and the cytochrome enzyme is liberated.

$$Hb - Fe^{3+} + Cyt - FeCN \rightleftarrows Hb\ FeCN + Cyt - Fe^{3+}$$

Actual detoxication is then achieved by the administration of thiosulphate which, under the influence of sulfurtransferase, reacts with cyanide to form thiocyanate (SCN), a relatively non-toxic substance which is readily excreted in the urine.

$$Na_2\ S_2\ O_3 + CN \xrightarrow[SCN - oxidase]{sulfurtransferase} SCN + Na_2\ SO_3$$

The disadvantages of this method are:
1) possibility of marked hypotension,
2) possibility of hypoxia by creating a concentration of methemoglobin of such magnitude that normal oxygen transport is impaired. Transfusion may be required to rectify such a situation.

b) Use of Cobalt EDTA[2]
Cobalt EDTA reacts with cyanide to form cobalticyanide $Co\ (CN)_6^{-3}$ and monocobalt EDTA both of which are excreted in the urine within 24 hours of administration.

The usual procedure is to inject intravenously 20 mls (300 mg) of kelocyanor (Cobalt EDTA – available from Laboratories LaRoche Nevaronne of Paris). This injection may be repeated. The oxygen carrying capacity of hemoglobin is not compromised with this treatment. However, should this drug be given to people who were not exposed to cyanide, and therefore have no cyanide in their system, then nausea, vomiting, sweating and ventricular etopic beats may occur as a result

of treatment. Cases so mistakenly treated have required intensive care.[3]

In general, antidotes should only be given to patients who are either unconscious or losing consciousness. This decision should be made by the attending physician who is capable of differentiating cyanide poisoning from such conditions as diabetes, myocardial infarction, cerebral vascular accidents and others. An appropriate guide for cyanide users, first aiders, and physicians is given in the Appendix. Physicians who supervise plants where the possibility of cyanide poisoning exists, should contact Dr. Graham (Food and Drug, Ottawa) telephone 613-922-4684 and seek approval to obtain and administer Cobalt EDTA.

Requests for reprints should be addressed to:
Dr. Ihor Taraschuk,
Medical Consultant,
Occupational Health Branch,
Ministry of Labour,
400 University Avenue,
7th Floor,
TORONTO, Ontario
M7A 1T7

References:

[1]Thorn G.W., et al, editors; *Harrison's Principles of Internal Medicine*, McGraw Hill Book Co., Eth ed; 1977 p. 695.

[2]Hillman, B.; et al; *The use of dicobalt edetate (Kelocyanor) in cyanide poisoning* Post Grad. Med. Journal (March 1974) *50*, p. 171-174.

[3]Bryson, D.D., et al *Cyanide Poisoning*: The Lancet 1978, p. 92.

Appendix

Cyanide Poisoning

Hydrogen Cyanide and Derivatives:
Sodium cyanide, calcium cyanide, potassium cyanide, acrylo-nitrile, cyanogen chloride, cyanides and nitro-prussides.
These solids, liquids and gases are deadly. Some act rapidly.

Poisoning may result from:
1. Breathing of gas, mist or dust
2. Swallowing
3. Skin absorption including eye splashes

Symptoms and Signs of Poisoning:
Weakness, nausea, dizziness and throat irritation. The symptoms may be delayed. **Collapse and death may result**.

Special Precautions:
Cyanides should be handled only by trained workers.

1. Containers should be clearly labelled: **Danger!** May be fatal if swallowed, inhaled or absorbed through skin.

2. Wash before: eating, smoking, drinking, and using toilet facilities.

3. Smoking, eating and drinking must be prohibited in areas where cyanide is handled.

4. Work clothes should be changed frequently and washed separately.

5. Cyanide compounds should be stored away from moisture and acid, since either moisture or acid may react with cyanide compounds to produce hydrogen cyanide gas.

6. First aiders should be available in the plant at all times. They should be trained in cardio-pulmonary resuscitation including the use of bag-mask oxygen respirators.

First Aid

Speed and medical attention is essential

Note to first aiders:

1. Make sure rescuer is safe –
wear a respirator if there is danger of inhalation, wear protective clothing if there is danger of skin absorption.

2. Remove victim from exposure. Call ambulance and physician

3. *Check for breathing*
a) if *not* breathing, begin artificial respiration using bag-mask oxygen respirator.
b) If breathing, keep under close observation.

4. *Check for consciousness*
a) If *unconscious or losing consciousness*, break capsule of amyl nitrite into a handkerchief and let patient inhale for 15 seconds. Repeat with fresh capsule every 3 minutes up to 6 capsules. Monitor blood pressure. If systolic pressure falls below 90 stop inhalations. If breathing stops, start artificial respiration (using bag-mask oxygen respirator).
b) If *conscious*, remove soiled clothing. Wash contaminated areas with water for at least 15 minutes.

5. If it is suspected or known that cyanide has been *swallowed*, and the victim is *conscious*, prepare the Iron Salt Antidote by mixing solutions A & B in equal proportions in a tumbler and give by mouth.

6. *Transfer to hospital* – Take emergency kit and instructions with the patient.

Note to Physician:
If *unconscious or losing consciousness* give intra-venous therapy
a) Withdraw 10 ml of blood for laboratory estimation of blood cyanide level

b) Inject *either*
i) 20 mls of Kelocyanor intravenously. Repeat with a further 20 mls of Kelocyanor followed by 50 ml of dextrose solution (50% solution)
The initial effect of the injection is a fall in blood pressure, a rise in pulse rate and sometimes retching. Immediately after this phase, lasting about one minute,

the patient should show signs of recovery, unless the absorbed dose of cyanide has been very large.

or

ii) 10 mls of 3% sodium nitrite solution intravenously (slowly over 4 minutes) followed by 50 mls of 25% thiosulphate intravenously (slowly over 10-15 minutes). Monitor methemoglobin and blood pressure.

Emergency Kit

Must contain:

1. Iron Salt Antidote

   Solution A – 158 gm hydrated ferrous sulphate ($FeSO_4 7H_2O$) and 3 gm citric acid dissolved in water and diluted to 1,000 ml
   (shelf life of one month)

   Solution B – 60 gm of anhydrous sodium carbonate (Na_2CO_3) dissolved in water and diluted to 1,000 ml
   (shelf life of 12 months)

   Dose: Mix about 50 ml of A with 50 ml of B in a tumbler and give through the mouth.

2. 6 capsules of amyl nitrite
   (shelf life of 24 months)

3. 2 × 10 ml ampoules sodium nitrite (3% solution)
   (shelf life 24 months)
   2 × 50 ml ampoules sodium thiosulphate
   (25% solution) (shelf life 6 months)
   4 × 20 ml ampoules of Kelocyanor –
   (shelf life 24 months)
   2 × 50 ml ampoules of dextrose injection
   (50% solution) (shelf life 24 months)

4. 2 × blood specimen containers (vacuum with heparin or oxalate)

5. Bag-mask oxygen respirator with oxygen supply

6. Blood pressure cuff and stethoscope.

Symposium on Measurement and Control of Chemical Hazards in the Workplace Environment

Sponsored by
The Division of Chemical Health and Safety of the American Chemical Society

The symposium is planned for the American Chemical Society's 180th National Meeting to be held in San Francisco, California, August 25-28, 1980. The purpose of the symposium will be to assess the state-of-the-art and future directions of monitoring and measurement procedures of the occupational environment and will encompass topics such as:

1. New analytical techniques and method development efforts.

2. Occupational environmental monitoring and control technology including medical monitoring and analysis.

3. Quality assurance and requirements of compliance statistics.

The technical program will comprise both invited and contributed papers, and both authoritative reviews and original research papers will be considered. A 20-minute presentation time will be allowed for a contributed paper while the duration for the presentation of an overview paper will be 40 minutes. Persons wishing to present a paper should submit a 200 word abstract on standard ACS abstract form by March 24, 1980. However, the prospective authors are urged to send their intention to present a paper as soon as possible. Abstracts and all technical inquiries should be directed to:

Dr. Gangadhar Choudhary, Symposium Chairman
National Institute for Occupational Safety and Health
DPSE, Mail Stop R-3
4676 Columbia Parkway
Cincinnati, Ohio 45226
(U.S.A.)
Telephone: AC 513, 684-4217

The abstract forms will be mailed to each participant after the intention to present is indicated.

The authors will be notified of the acceptance of their papers for presentation immediately after receipt of the abstract. It is planned to chronicle the proceedings in a book form published either by the ACS or by a renowned publisher. The decision to publish will be made after the abstracts have been reviewed. To facilitate this decision the abstract should be informative regarding the content and main conclusions of the paper. Depending upon the decision, the authors will be notified of the deadline for submission of their manuscripts.

Book Review

Edited by A. Ward Gardner
Publishers John Wright & Sons Ltd.
Bristol 1979
$48.00

Current Approaches to Occupational Medicine

The editor of this book, an experienced writer and occupational physician has collated 22 papers with a view to illuminating some current problems, to give perspective and to review progress – mainly in the field of occupational health, occupational medicine and occupational hygiene. A worthy aim but inevitably this book of 'short stories' suffers from a lack of continuity in content, as well as author style. This may or may not please you. Personally, I feel it detracts. Readers who keep themselves up-to-date with current publications will find little to excite them, but most of the chapters are current reviews and therefore provide useful reading. The topics discussed range from toxicology and training, to screening and stress, so are very wide ranging. The chapters on lead, other metals, man-made mineral fibres, and gases are good textbook reading, while those on respiratory disorders, stress and toxicity testing are lucid and stimulate interest. Of particular value to Canadian readers will be the chapters on nursing, alcohol related disabilities and sickness absence. All in all, this publication is a useful addition to the small library of books dealing with occupational medicine but peruse the library copy first before you buy.

Peter L. Pelmear

News and Notes

A guide for the preparation of a policy and procedure manual for occupational health nurses has been prepared by the Occupational Health Branch, Ministry of Labour.

This manual will be distributed by the nursing consultants of the branch.

Ontario
Ministry of
Labour

Occupational
Health and Safety
Division

Occupational
Health Branch

400 University Ave.
Toronto, Ontario
M7A 1T7

Telephone:
(416) 965-3610

ISSN 0705-9388